First author, year [reference]	No. of patients	Magnetic field, system / MRI sequence	Preprocessing of MRI images	Deep learning method / RR or DR / 2D or 2.5D or 3D training	Overall loss function (for GANs) or generator loss function	Adversarial loss used by discriminator (for GANs)	No. of patients in training / evaluation	Image and g	leometry fi	idelity re	esults	Dose results
Han et al., 2017 [1]	18	1.5 T Siemens / 3D T1	N3 bias field correction algorithm, histogram matching	DCNN: U-Net / RR / 2D	L1 loss	-	15 (6-fold cross validation)/ 18	MAE [HU] 84.8 ± 17.3	<b>МЕ [ŀ</b> -3.1 ±	<b>HU]</b> 21.6	<b>MSE</b> [HU <sup>2</sup> ] 188.6 ± 33.7	/
<b>Nie et al., 2017</b> [2]	16	3 T Siemens /	/	GAN (with FCN for generator and CNN for discriminator) / ❖/ 3D	L2 loss + gradient loss + adversarial loss	Binary cross entropy	15 (leave- one-out) / 16	<b>MAE [HI</b> 92.5 ± 13	.9	<b>PSN</b> 27.6	<b>R [dB]</b> 5 ± 1.3	/
Wolterink et al., 2017 [3]	24	1.5 T Philips / 3D T1	/	Cycle-GAN / RR / 2D	Least squares loss + adversarial loss + gradient difference loss + cycle consistency loss (based on L1 norm)	Binary cross entropy	18 / 6	MAE [HI 73.7 ± 2.	3 J	<b>PSN</b> 32.5	<b>R [dB]</b> 5 ± 0.7	/
Dinkla et al., 2018 [4]	52	1.5 T Philips / pre contrast 3D T1	3D geometry correction provided by the vendor + intensity normalization	Dilated CNN / RR 2.5D	L1 loss		26 (two- fold cross validation)/ 52	MAE [HU] Body = $67 \pm 11$ Soft tissue = $22$ $\pm 3$ Bone = $174 \pm 29$ Air = $159 \pm 22$	ME [H Body = 7 Soft tissue 3 Bone = 7 Air = -77	<b>IU]</b> 13 ± 9 e = -2 ± 75 ± 41 1 ± 27	DSC Body contour = 0.98 ± 0.01 Bone = 0.85 ± 0.04 Air = 0.71 ±	Mean dose difference < 1% $\gamma \Box = 91.1\%$ $\gamma * = 95.8\%$ $\gamma^{**} = 99.3\%$

										0	.07	
Emami et al., 2018 [5]	15	1 T Philips / Post- Gadolinium T1	/	GAN (ResNet for generator and CNN for discriminator) / RR / 2D	L1 loss + adversarial loss	Least square loss	12 (5-fold cross validation) / 15	MAE [HU] Head = $89.3 \pm 10.3$ Soft tissue = $41.9 \pm 8.6$ Bone = $255.2 \pm 47.7$ Air = $240.9 \pm 60.2$	<b>PSNR [dB</b> Head = 26.0 1.2	8] SSI 6 ±Head = ± 0.0	<b>M</b> ⊧ 0.83 03	/
Xiang et al., 2018 [6]	16	3T Siemens / T1	N3 bias field correction algorithm, intensity histogram matching, intensity normalization	DECNN / RR / 3D	L2 norm + L2-norm of embedding blocks	-	15 (leave- one-out) / 16	<b>MAE [H</b> ] 85.4 ± 9	U] .2	<b>PSNR [d</b> 27.3 ± 1	<b>B]</b> .1	/
Yang et al., 2018 [7]	45	1.5 T Siemens / �	3D distortion correction algorithm (vendor) + N4 correction + intensity normalization	Cycle-GAN / � / 2D	Adversarial loss, cycle- consistency loss (L1 norm), structure consistency loss (L1 based on MIND)	Binary cross entropy	27 / 15	MAE [HU] 129	<b>PSNR [dB</b> 24.2	8] SSI 0.7	<b>M</b> 8	/
Gupta et al., 2019 [8]	60	3T Siemens / T1 with Dixon	/	U-Net / RR / 2D	Combination of L1 loss: MAE + MSE	-	47 / 13	All vox Soft tis Bone Air	MAE [HU] kels = 81.0 ± ssue = 17.6 e = 193.1 ± 3 = 233.8 ± 28	= 14.6 ± 3.4 38.3 3.0		For 7 patients: D <sub>mean</sub> PTV difference = 2.3%

Kazemifar et al., 2019 [9]	77	1.5 T � / Post- Gadolinium 2D T1	/	cGAN / RR / 2D	Mutual information	Binary Cross entropy	70% of 77 / 1% of 77	Average cross vali [ł 47.2	MAE over dation sets IU] ± 11.0	Head Bond Air = 0	<b>DSC</b> d = 0.96 ± 0.02 e = 0.80 ± 0.06 0.70 ± 0.07	Dose differences < 2.4% for PTV and OARs $\gamma \square = 94.6\%$ $\gamma * = 99.2\%$
					MAE			60.2	± 22.0		1	/
Koike et al., 2019 [10]	15	Philips, GE and Siemens / T1, T2 and FLAIR	N4 bias field correction algorithm	cGAN / DR / 2D	Adversarial loss + L1 loss	Binary cross entropy	12 (5-fold cross validation) / 15	So I So	MAE [H           T1w sequ           Body = 120.           oft tissue = 4           Bone = 399.           All seque           Body = 108.           ft tissue = 3           Bone = 366.	<b>iU]</b> ience $1 \pm 20.4$ $46.3 \pm 9.3$ $4 \pm 51.8$ ences $1 \pm 24.0$ $8.9 \pm 10.2$ $2 \pm 62.0$	3	Dose difference < 1% <i>T1w sequence</i> $\gamma \Box = 94.2\%$ $\gamma * = 98.9\%$ $\gamma * = 99.7\%$ <i>All sequences</i> $\gamma \Box = 95.3\%$ $\gamma * = 99.2\%$ $\gamma * = 99.8\%$
Lei et al., 2019 [11]	24	♦ GE / T1- BRAVO	N3 bias field correction algorithm + intensity normalization	Cycle-GAN / RR / 3D	Adversarial loss + distance loss (combination of Mean P Distance and Gradient Difference)	MAD	23 (leave- one-out) / 24 24/10	MAE [HU] 55.7 ± 9.4 57.7 ± 8.4	<b>PSNR</b> [dB] 26.6 ± 2.3 27.0 ± 2.8	NCC 0.96 ± 0.01 0.96 ± 0.01	DSC Air = 0.90 ± 0.12 Bone = 0.83 ± 0.06 /	/
Liu et al., <b>2019</b> [12]	50	1.5 T GE / 3D T1 BRAVO + 1,5 T GE / post-contrast T1	/	DCNN / DR / 2D	MSE	-	40 / 10	<b>MAE</b> 75	<b>[HU]</b> ± 23	Sof 0.9 Bone	<b>DSC</b> t tissue = $4 \pm 0.02$ e = 0.85 ± 0.02	Absolute mean dose difference < 1.5% $\gamma^{**}_{**} = 99.2\%$

									Air =	= 0.95 ± 0.01	
				U-Net / RR / 2D				<b>MAE [HU]</b> 55 ± 10		ME [HU] -1 ± 4	$\begin{array}{r} \gamma \square = 95\% \\ \gamma \ \ast \ = 98\% \end{array}$ Protontherapy: Range difference of 3 mm < 5% of the profiles $\gamma \ \ast \ = 91.7\%$
Neppi et al., 2019 [13]	89	/ T1 MPRAGE	/	U-Net / RR/ / 3D	*	-	57 / 4	90 ± 20		11 ± 9	$\begin{array}{l} \gamma \square = 95\% \\ \gamma \ ^{\ast} = 98\% \end{array}$ $\begin{array}{l} Proton therapy: \\ Range \ difference \ of \ 3 \\ mm \ < 5\% \ of \ the \\ profiles \end{array}$ $\begin{array}{l} \gamma \ ^{\ast} = 89.3\% \end{array}$
Shafai-Erfani et al., 2019 [14]	50	1.5 T Siemens / 3D T1	N4 bias correction filter	Cycle-GAN / RR / 3D	Adversarial loss, MAD (L1 norm), Mean P distance and gradient- difference loss	Mean P distance : lp norm	25 / 25	<b>MAE [HU]</b> 54.6 ± 6.8	0	NCC .96 ± 0.01	Protontherapy: Dose difference < 0.5% Mean distal range: 1.1 $\pm 0.9 \text{ mm}$ $\gamma \square = 89.2\%$ $\gamma * = 98.1\%$ $\gamma * = 99.9\%$
Spadea and Maspero et al., 2019 [15]	15	3 T Siemens / 3D T1	/	DCNN: U-Net / RR / 2.5D	L1 loss	_	14 (leave- one-out) / 15	MAE [HU]MBody = $54 \pm 7$ BodyCerebrospinalCerefluid = $10 \pm 3$ fluidGray matter =Gray $8 \pm 2$ White matter =White 2White	<b>ME [HU]</b> $y = -4 \pm 17$ ebrospinal id = 0 ± 9 iy matter = 0 ± 6 te matter = 0 ± 4	DSC Bone = 0.93 ± 0.02 Air = 0.92 ± 0.03	Protontherapy: PTV dose difference < 0.1 Gy Relative range shift: 0.14 ± 1.11%

								$Air = 53 \pm 3$	32 Air = -37	± 39		
Alvarez Andres et al., 2020 [16]	402	1.5 T + 3 T GE / T1 and FLAIR	N4 filter	CNN (HighResNet)/ RR / 2D		-	242 / 79		MAE [HU Head = 81 ± Water = 38 ± Bone = 228 ± Air = 274 ±	] ⊧ 22 ⊧ 11 ± 63 63		Dose differences: PTV ( $D_{2\%}$ , $D_{50\%}$ , $D_{95\%}$ , $D_{98\%}$ ) < 0.3% $\gamma \square = 97.9\%$ $\gamma * = 99.6\%$ $\gamma * = 99.8\%$
				U-Net / RR / 3D	MAE	-			<b>MAE [HU</b> Head = 90 ±	] : 21		γ** = 99.7%
Hemsley et al., 2020 [17]	105	1.5 T Philips / T1 and FLAIR	MR normalization	cGAN (pix2pix)/ RR / 2D	adversarial + log- likelihood of the Laplace distribution	Binary cross entropy	85 / 20	Nor Air-bo	MAE [HU mal soft tissue one interface =	] e = 6 ± 3 = 237 ±	3 31	/
Kazemifar et al., 2020 [18]	77	1.5 T � / 2D T1	/	cGAN / no registration / 2D	Mutual information	Binary cross entropy	54 / 11	Average MAE over all-cross validat sets [HU] 47.2 ± 11.0 MAE [HU] PSNR [dB] SSIM MS			alidation	Protontherapy: Mean dose difference < 1.8% Up to 5.1% for brainstem D <sub>2%</sub>
				U-Net / RR /	L1	-		MAE [HU] 75.5 ± 7.9	<b>PSNR [dB]</b> 25.4 ± 0.6	<b>SSIM</b> 0.94 ± 0.01	$MSE [HU] 4.9.10^{4} \pm 7.7.10^{3}$	
Li et al., 2020 [19]	34	1.5 T Siemens / T2	Distorsion correction	20	L2 L1 + L2		28 / 6	$/6 \qquad 75.5 \pm 11.7 \qquad 32.2 \pm 1.1 \qquad \begin{array}{c} 0.94 \pm \\ 0.01 \qquad 3.1.10^{3} \\ 0.01 \qquad 3.1.10^{3} \\ 0.01 \qquad 2.4 \pm 0.94 \pm \\ 0.01 \qquad 2.4 \pm 0.94 \\ 0.01 \qquad 2.4 \pm 0.94 \\ 0.01 \qquad 0.01 \qquad 0.01 \\ 0.01 \\ 0.01 \qquad 0.01 \\ 0.01 \\$	/			
				cGAN (pix2pix) / RR / 2D	*	*		94.6 ± 17.2	30.3 ± 1.2	0.91 ± 0.01	$1.6 \cdot 10^4 \pm 4.9 \cdot 10^3$	
				Paired Cycle- Gan / RR / 2D	*	*		87.7 ± 7.9	30.9 ± 0.6	0.92 ± 0.00	$1.4 \cdot 10^4 \pm 2.1 \cdot 10^3$	

				Unpaired Cycle-Gan	*	*		98.7 ± 12.7	29.9 ± 0	.9 0.91 <u>-</u> 0.01	$\pm 1.7 \cdot 10^4 \pm 3.3 \cdot 10^3$	
Liu et al., <b>2020</b> [20]	15	1.0 T Philips / Postgadolinium T1	/	GAN (ResNet for generator and CNN for discriminator) / RR / 2D	L1 loss + adversarial loss	L2 loss	12 / 3 (5- fold cross validation)	E	mami et a	<b>I., 2018</b> [5]	l	Dose differences: PTV and OARs < 0.13 Gy γ□= 99.0% γ * = 99.9%
Maspero et al., 2020 [21]	60 (paediatric patients)	1.5 T and 3 T Philips / 3D T1	MRI was normalised and clipped to their 99 <sup>th</sup> percentile intensity over the whole volume	cGAN / RR / 2D	L1 loss	*	30 / 20 (4- fold cross- validation)	MAE [HU] 61.0 ± 14.1	<b>PSNR</b> [dB] 26.7± 1.9 dB	<b>SSIM</b> 0.86±0.03	DSC Body = 0.984 ± 0.004 Bone = 0.92 ± 0.05	Photontherapy:Dose differences <
Massa et al., 2020 [22]	92	1.5 T GE / T1w, T2- FatSat, T1 Post contrast, T2 CUBE FLAIR	/	U-net with Inception V3 inspired blocks / DR / 2D	*	-	81 / 11	<b>MAE [HU]</b> T1w: Brain = $51.2 \pm$ 4.5 Bone = $31.1 \pm 7.0$ T2-FatSat: Brain = $45.7 \pm 8.8$ Bone = $30.3 \pm 7.1$ T1 Post contrast: Brain = $44.6 \pm 7.5$ Bone = $30.2 \pm 6.0$	<b>PSNR</b> [dB] T1w: Brain = $43.0 \pm 2.0$ Bone = $43.2 \pm 1.9$ T2- FatSat: Brain = $43.4 \pm 1.2$ Bone = $43.7 \pm 1.2$	<b>SSIM</b> T1w: Brain = $0.65 \pm$ 0.05 Bone = $0.87 \pm$ 0.03 T2- FatSat: Brain = $0.63 \pm$ 0.03 Bone = $0.86 \pm$ 0.02 T1 Post	DSC T1w: Soft tissue = $0.91 \pm$ 0.03 Bone = $0.76 \pm$ 0.12 T2- FatSat: Soft tissue = $0.91 \pm$ 0.02 Bone = $0.77 \pm$ 0.07	/

								T2 CUBE FLAIR: Brain = 51.2 ± 4.5 Bone = 36.1 ± 3.3	T1 Post contrast: Brain = $43.4 \pm$ 1.2 Bone = $43.7 \pm$ 1.2 T2 CUBE FLAIR: Brain = $44.9 \pm$ 1.2 Bone = $45.2 \pm$ 1.1	contrast: Brain = 0.64 ± 0.03 Bone = 0.86 ± 0.03 T2 CUBE FLAIR: Brain = 0.61 ± 0.04 Bone = 0.84 ± 0.02	T1 Post contrast: Soft tissue = $0.90 \pm$ 0.02 Bone = $0.75 \pm$ 0.07 T2 CUBE FLAIR: Soft tissue = $0.88 \pm$ 0.03 Bone = $0.69 \pm$ 0.07	
<b>Tang et al., 2020</b> [23]	37	3 T Siemens / T1 TIRM	/	cGAN (pix2pix)/ RR /	MAE + adversarial loss	Least square loss	27 (5 fold cross- validation) / 10	MAE [HU] 60.5 ± 13.3		<b>PSNR [dB</b> 49.2 ± 1.9	)	Dose differences: PTV < 0.13% Brainstem, optic chiasma, optic nerve < 0.77% $\gamma _{*}^{*} = 97.3\%$ $\gamma_{**}^{**} = 99.8\%$
Bourbonne et al., <b>2021</b> [24]	184	1.5 T Siemens / T2 and post gadolinium 3D T1	MRI voxel intensities were clipped to be inside the [1-99%] quantile range.	cGAN (pix2pix) / � / 2D	Adversarial loss and MAD (L1 norm)	PatchGAN	20 / 164	Sof B	RMSE it-tissue = one = 175	<b>[HU]</b> 13.54 ± 1.9 .50 ± 63.18	96	Dose differences: PTV < 0.4 Gy Local γ * = 99.1%

Additional table 1: Synthetic-CT generation from brain MRI in the literature: summary of data, deep learning architecture, and image and dose evaluations

 $\gamma \Box = 1\%/1$  mm gamma pass-rate 1%/1mm;  $\gamma * = 2\%/2$  mm gamma pass-rate;  $\gamma * = 3\%/3$  mm gamma pass-rate;  $\diamondsuit =$  not specified in the study Abbreviations: GAN = generative adversarial network, MAD = mean absolute distance, MAE = Mean Absolute Error; ME = Mean Error; DSC = Dice Similarity Coefficient; PSNR = Peak Signal-to-Noise Ratio; SSIM = Structural Similarity; NCC = Normalized Cross-Correlation; MSE = Mean Square Error; RR = Rigid Registration; DR = Deformable Registration; DECNN = Deep Embedding Convolutional Neural Network; DCNN = Deep CNN.

First author, year [reference]	No. of patients	Magnetic field, system / MRI sequence	Preproces sing of MRI images	Deep learning method / RR or DR / 2D or 2.5D or 3D training	Overall loss function (for GANs) or generator loss function	Adversaria I loss used by discriminat or (for GANs)	No. of patients in training / evaluation	Imaę	ge and geometr	ic fidelity	r results	Dose results
Dinkla et al., 2019 [25]	34	3 T Philips / T2 - Dixon	2D geometry correction + uniformity correction (CLEAR)	U-Net / DR / 3D	L1	-	22 (3-fold cross validation) / 34	<b>MAE</b> [HU] Body = 75 ± 9	<b>ME [HU</b> Body = 9 =	<b>]]</b> ⊧ 11	DSC Bone = 0.70 ± 0.07 Air = 0.79 ± 0.08	Dose difference < 1% γ * = 95.6% γ** = 98.7%
Klages et al., 2019 [26]	20	3 T Philips / mDixon T1 Fast Field Echo (FFE)	Intensity inhomoge neity correction (CLEAR)	cGAN (Pix2Pix) / DR / 2D cycle-Gan / DR / 2D	Adversarial loss + Absolute differences (L1)	Binary cross entropy	10 / 10	MA Body = Body = 1	<b>E [HU]</b> 92.4 ± 13.5 100.7 ± 14.6	N Body Body =	<b>AE [HU]</b> = 21 ± 11.8 = 37.5 ± 14.9	Dose differences: PTV <sub>70Gy</sub> < 0.8% OARs < 2% Dose differences: PTV <sub>70Gy</sub> < 1.6% OARs < 1.7%
Wang et al., <b>2019</b> [27]	33	1.5 T Siemens / T2 TSE	Histogram matching	DCNN: U- Net / RR and DR / 2D	L2: MSE	-	23 / 10	MA Body =	<b>E [HU]</b> = 131 ± 24	N Body	<b>ME [HU]</b> y = −6 ± 13	For one patient: PTV D <sub>98%</sub> difference < 1%

Largent et al., <b>2020</b> [28]	8	1.5 T GE / 3D T2	N4 bias- field correction and histogram matching	GAN / RR and DR / 2D	Perceptual loss	Cross entropy	7 (leave- one-out) / 8	5	<b>MAE [HU]</b> 32.8 ± 48.6	6	<b>ME [⊦</b> -3.9 ± ′	<b>U]</b> 2.8	/
<b>Peng et al.,</b> <b>2020</b> [29]	173	3 T Philips / T1	Intensity of each MR volume image was normalize d as zero mean and unit variance and then scaled to a similar numeric range	cGAN (registered pairs) / DR / 2D cycle-Gan (unregistered pairs) / - / 2D	Adversarial loss + L1 loss Cycle- consistency loss (MAE loss) + adversarial loss + L1 loss	Least square loss PatchGAN loss	135 pairs / 28 pairs	Body	<b>MAE [HU]</b> y = 69.7 ± y = 100.6 =	1 : 9.3 ± 7.7	<b>ME [H</b> Body = 18. Body = 6.7	<b>U]</b> 4 ± 16.4 <sup>-</sup> ± 19.4	Dose differences: PTV ( $D_{95\%}$ ) < 0.7% Parotids ( $D_{mean}$ ) < 0.9% Mandible ( $D_{max}$ ) < 1.5% $\gamma * = 98.7\%$ $\gamma * = 99.6\%$ Dose differences: PTV ( $D_{95\%}$ ) < 0.9% OARs ( $D_{mean}$ ) < 1.2% Mandible ( $D_{max}$ ) < 1.6% $\gamma * = 98.5\%$ $\gamma * = 99.6\%$
Qi et al., 2020 [30]	45	3 T Philips / T1, T2, contrast-	Normaliza tion to [-1, 1] based on the minimum	cGAN / RR / 2D	Adversarial loss + L1 loss	PatchGAN loss	30 / 15	MAE [HU] Body : T1 = 75.2 ±	<b>ME</b> [HU] Body : T1 = 1.3 ±	<b>PSNR</b> [dB] T1 = 28.9 ± 1.1	<b>SSIM</b> T1 = 0.84 ± 0.02	<b>DSC</b> Bone: T1 = 0.74 ±	Dose difference < 1% T1: γ * =

		enhanced T1 (T1C) and contrast- enhanced T1 with Dixon (T1Dixon C)	and maximum intensity values						8  8  8  7	11.5 T2 = $87.0 \pm$ 10.8 T1C = $80.0 \pm$ 10.9 T1Dix onC = $86.3 \pm$ 10.8 Multis eq. = $70.0 \pm$ 12.0	14.9 T2 = 12.3 ± 16.2 T1C = 5.0 ± 16.0 T1Dixo nC = 6.4 ± 16.7	T2 = ± T1 28 1 T1E C = ± Mult = 2! 1	= 27.5 0.9 C = .4 ± .1 Dixon 27.7 0.9 tiseq. 9.4 ± .3	$T2 = 0.78 \pm 0.03$ $T1C = 0.82 \pm 0.03$ $T1Dixo nC = 0.79 \pm 0.03$ Multise q. = 0.85 \pm 0.03	$\begin{array}{c} 0.05 \\ T2 = \\ 0.68 \pm \\ 0.05 \\ T1C = \\ 0.72 \pm \\ 0.05 \\ T1Dixo \\ nC = \\ 0.69 \pm \\ 0.06 \\ \end{array}$ Multise q. = 0.77 \pm \\ 0.05 \\ \end{array}	97.4% T2: $\gamma * =$ 95.8% T1C: $\gamma * =$ 96.7% T1DixonC: $\gamma * = 96.2\%$ Multiseq.: $\gamma * = 97.8\%$
				U-Net / 2I	/ RR D	L1 loss	-		7	71.3 ± 12.4	/	29 1	.2 ± .3	/	0.76 ± 0.05	Dose difference < 0.9% γ * = 97.6%
Thummerer et al., 2020 [31]	27	3 T Siemens / 3D spoiled gradient recalled echo	/	DCNN 2.5	/ DR / D	L1 loss	-	18 (3 cro valida / 2	3-fold oss ation) 27	<b>M</b> Body	<b>AE [HU]</b> = 65.4 ±	3.6	B	<b>ME [HU</b> ] Body = 2.9 ±	l = 9.4	Protontherap y: Range errors > 3% γ * = 97.6%
Tie et al., 2020 [32]	32	1.5 T Siemens / T1 precontra st + T1 postcontr ast and T2	N4 bias co algorith histogr normaliz	rrection m + am ation	cGAN (Pix2Pi x) / RR / 2D	Combination of Pearson f- divergence + adversarial los + L1 loss	of Least squar loss	2 e va	8 (8-fold cross alidation) / 32	М/ [Н Неа 75. 14	AE F U] ad = 7 ± 1.6	<b>PSNR</b> 29.1 ±	<b>[dB]</b> 1.6	DSC Bone = 0.86 ± 0.03	SSIM 0.92 ± 0.02	/

Palmér et al., 2021 [33]	44	1.5 T Siemens / T1w Dixon Vibe	*	Deep CNN / RR + DR / 2D	*	-	80 (multicent er database) / 44	MAE [HU] Body = 67 ± 14	<b>ME [HU]</b> Body = -5 ± 10	DSC Bones = 0.80 ± 0.07 Air =0.81 ± 0.1	HD [mm] Bones = 4.6 ± 1.2 Air = 2.8 ± 0.8	Mean dose differences PTV and OARs < 0.3% γ (2%/1 mm)=99.4%
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Additional table 2: Synthetic-CT generation from head and neck MRI in the literature: summary of data, deep learning architecture, and image and dose evaluations

 $\gamma = \frac{2\%}{2}$  mm gamma pass-rate;  $\gamma = \frac{3\%}{3}$  mm gamma pass-rate;  $\diamondsuit =$  not specified in the study.

Abbreviations: GAN = generative adversarial network, MAE = Mean Absolute Error; ME = Mean Error; HD = Hausdorff distance, DSC = Dice Similarity Coefficient; PSNR = Peak Signal-to-Noise Ratio; SSIM = Structural Similarity; RR = Rigid Registration; DR = Deformable Registration; MSE = mean square error, DCNN = Deep Convolutional Neural Network.

First author, year [reference]	Anatomical site	No. of patients	Magnetic field, system / MRI sequence	Preprocessing of MRI images	Deep learning method / RR or DR / 2D or 2.5D or 3D training	Overall loss function (for GANs) or generator loss function	Adversarial loss used by discriminator (for GANs)	No. of patients in training / evaluation	Image and g	geometric fidelity esults	Dose results
<b>Jeon et al.,</b> <b>2019</b> [34]	Breast	16	0.35 T, MRIdian (Viewray) / �	/	U-Net / DR / 2D	Binary cross- entropy	-	14/2	D Patie Patie	<b>SC (%)</b> nt 1 = 76.4 nt 2 = 73.5	/
Liu et al., 2019 [35]	Liver	21	3 T Skyra / 3D T1 + 3 T TrioTim Siemens / T1 VIBE and 1.5 T GE / 2D T1	N4 bias field correction algorithm	cycle-GAN / DR / 3D	Weighted summation of adversarial loss and mean p distance (lp norm) + gradient difference	MAD	20 (leave-one- out) / 21	MAE [HU] Body = 72.9 ± 18.2	<b>PSNR [dB]</b> 22.4 ± 3.6	Protontherapy: PTV <sub>45Gy</sub> and bowel dose difference < 1 Gy PTV D <sub>95%</sub> < 1.1% Mean of absolute maximum range shift: 1.86 ± 1.55 mm $\gamma \Box = 90.8\%$ $\gamma _* = 97.0\%$ $\gamma _* = 99.4\%$
Liu et al., 2019 [36]	Liver	21	3 T Skyra/ 3D T1 + 3 T TrioTim Siemens / T1 VIBE and 1.5 T GE / 2D T1	N4 bias field correction filter	cycle-GAN / RR and DR / 3D	Weighted summation of MAD (adversarial loss) and mean p distance (lp norm) + gradient	MAD	20 (leave-one- out) / 21	MAE [HU] Body = 72.9 ± 18.2	<b>PSNR [dB]</b> 22.7 ± 3.6	Mean dose difference: PTV D <sub>95%</sub> = 0.2% Dose difference to OARs < 0.06 Gy

						difference							γ□ = 99.0%
<b>Olberg et al.,</b> <b>2019</b> [37]	Breast	48	0.35 T Viewray / T1	Histogram matching	U-Net and ASPP / DR / 2D	Adversarial (Cross entropy loss) + MAE	Cross entropy loss	48 / 12	<b>RMSE</b> [HU] 17.7 ± 4.3	<b>PSN</b> [dB] 71.7 ±	<b>R S</b> I 0.9 2.3 0.	9995 ± 0003	For 4 patients PTV D <sub>95%</sub> < 0.9% γ * ≥ 98.0%
<b>Xu et al.,</b> <b>2019</b> [38]	Abdomen	10	♦ / mDixon	*	MCRcGAN (ResNet + multichannel cGAN) / DR / 2D	L1 loss + cGAN loss (cross entropy loss)	Cross entropy loss	9 (leave-one- out) / 10		<b>MAE</b> 60	<b>[HU]</b>		/
Cusumano et al., 2020 [39]	Pelvis and abdomen	60 pelvis / 60 abdominal	0.35 T MRIdian (Viewray) / T2/T1	*	cGAN (pix2pix) / DR / 2D	$\begin{array}{l} L_{GAN}+\lambda\cdot L1\\ \text{with }\lambda=100\\ L_{GAN}:\\ \text{adversarial}\\ \text{loss function} \end{array}$	*	40 pelvis, 40 abdomen/20 abdomen	MAE [HU]         ME (HU)           Body = 78.7 ±         Body = 10.8           18.5         ± 12.9				$\gamma \square = 90.8\%$ $\gamma * = 98.7\%$ $\gamma * = 99.8\%$
Florkow et al., <b>2020</b> [40]	Wilms' tumour (24) and Neuroblastoma (42)	66	1.5 T Philips / 3D T1 and 3D T2	Intensities clipped beyond the 95th percentile + resulting intensities linearly mapped to [-1; 1].	U-Net / DR / 3D	L1	-	54/12 (3- fold cross validation)	MAE [HU] Body = 57 ± 12 Lungs = 105 ± 34	ME [HU] Body = -5 ± 12 Lungs = -9 ± 67	<b>PSNR</b> (dB) Body = 30.3 ± 1.6	<b>DSC</b> (%) Bones = 76 ± 8 Lungs = 92 ± 9	Photontherapy: Mean dose difference <0.5% $\gamma * > 99\%$ Protontherapy: $\gamma * > 96\%$
Fu et al., 2020 [41]	Liver + Abdomen	12 (8 liver + 1 pancreas + 1 adrenal gland + 2 middle abdomen tumors)	0.35 T, MRIdian (Viewray) / True-FISP	N4 bias field correction algorithm + histogram normalization	cGAN / DR / 2D	cGAN + L1	Binary Cross entropy loss	9 (4-fold cross validation)/ 12	MAI Body 1	<b>E [HU]</b> = 89.8 = 8.7	<b>PSN</b> ± 27.	<b>IR [dB]</b> 4 ± 1.6	For 8 liver patients Dose difference:< 0.6% $\gamma * = 97.4\%$ $\gamma * = 99.5\%$

					cycle-GAN / DR / 2D	Adversarial loss + cycle consistency	Binary Cross entropy loss		Body = 94.1 ± 30	27.2 ± 2.2	For 8 liver patients Dose difference < 1% $\gamma * = 95.6\%$ $\gamma * = 99.3\%$
Liu et al., 2020 [42]	Abdomen	46	3 T Skyra Siemens/ 3D T1 ECHO	N4 Intensity inhomogeneity correction	U-Net / RR / 2.5D	*	-	31/46 (3 fold cross validation)	MAE [HU Liver = 24.1 = Kidneys = 47. Spinal Cord = 29 Lungs = 105.7	Mean dose difference < 0.15 Gy	
<b>Qian et al.,</b> <b>2020</b> [43]	Abdomen	10	◆ / mDixon	*	RU-ACGAN : hybrid network associated with AC-GAN and cGAN and combined with ResNet and U- Net simultaneously / DR /	L1 loss + adversarial loss	Binary cross entropy loss + Softmax loss	9/10 (leave- one-out)	<b>MAE [HU]</b> 55.6 ± 5.6	<b>RMSE [HU</b> ] 106.4 ± 12.2	/

Additional table 3: Synthetic-CT generation from breast, liver, and abdomen MRI in the literature: summary of data, deep learning architecture, and image and dose evaluations

 $\gamma \Box = 1\%/1 \text{ mm}$  gamma pass-rate 1%/1mm,  $\gamma \ddagger = 2\%/2 \text{ mm}$  gamma pass-rate,  $\gamma \ddagger = 3\%/3 \text{ mm}$  gamma pass-rate,  $\diamondsuit = \text{ not specified in the study}$ Abbreviations: MAE = Mean Absolute Error, PSNR = Peak to Signal-to-Noise Ratio, SSIM = Structural Similarity, NCC = Normalized Cross-Correlation, RMSE = Root Mean Square Error, MAD = mean absolute distance, GAN = generative adversarial network, ASPP = atrous spatial pyramid pooling, RU-ACGAN = Auxiliary classifier-augmented GAN.

First author, year [reference]	Anatomic al site	No. of patients	Magnetic field, system / MRI sequence	Preprocessing of MRI images	Deep learning method / RR or DR / 2D or 2.5D or 3D training	Overall loss function (for GANs) or generator loss function	Adversarial loss used by discriminator (for GANs)	No. of patients in training / evaluatio n	Image and geometric fidelity results				Dose results		
Nie et al., 2016 [44]	Pelvis	22	*	/	FCN / Manual alignment / 3D	*	-	21 (leave- one-out) / 22	<b>MAE [</b> Body = 4 5.1	HU] 12.4 ±	PSNI Body = 1	<b>₹ [dB]</b> = 33.4 ± .1	1		
Nie et al., 2017 [2]	Pelvis	22	*	*	GAN (with FCN for generator and CNN for discriminator)/ Manual alignment / 3D	L2 loss + gradient loss + adversarial loss	Binary cross entropy	21 (leave- one-out) / 22	MAE [HU] Body = 39.0 ± 4.6		Body = 39.0 ± 4.6		PSNR [dB] E Body = 34.1 ± 1.0		/
<b>Arabi et al.,</b> <b>2018</b> [45]	Prostate	39	3 T Siemens / 3D T2 SPACE	N3 bias field correction algorithm	DCNN: U-Net / RR and DR / 2D	MAE	-	(4-fold cross validatio n) <sup>3</sup> ⁄4 of 39 / 39	MAE [HU] Body = 32.7 ± 7.9	ME [HU] Body = 3.5 ± 11.7	<b>DSC</b> Bone = 0.93 ± 0.02	MASD [mm] Body = 1.8 ± 0.6	Mean dose difference < 0.5% Dose difference: CTV (D <sub>max</sub> ) = 2.9% OARs (D <sub>max</sub> )= 0.5% $\gamma \square = 94.6\%$ $\gamma * = 98.5\%$ $\gamma * = 99.2\%$		

<b>Chen et al.,</b> <b>2018</b> [46]	Prostate	51	3 T Philips / T2 TSE	No bias field correction and MR intensity histogram normalization	U-Net / DR / 2D	MAE	-	36 / 15	MAE [HU] Body = 30.0 ± 4.9	<b>ME [HU]</b> Body = 6.7 ± 5.4	Dose differences: 0.2% (PTV/OARs) $\gamma \square = 98.0\%$ $\gamma * = 99.4\%$ $\gamma * = 99.8\%$
	Prostate	59	3 T Philips / 3D Echo with Dixon					32 / 27	<b>MAE [HU]</b> Body = 65 ± 10	<b>ME [HU]</b> Body = 1 ± 6	For 10 patients /27 Dose difference: PTV (D <sub>98%</sub> )< 1% γ * = 95.0% γ** = 98.1%
Maspero et al., 2018 [47]	Rectum	18	3 T Philips / 3D Echo with Dixon	Normalized to their 95% intensity interval over the whole patient + converted to 8-bits	cGAN / RR / 2D	Adversarial loss + $\lambda$ ·L1 with $\lambda$ = 100	PatchGAN loss	32 (prostate patients) / 18	<b>MAE [HU]</b> Body = 56 ± 5	<b>ME [HU]</b> Body = 2 ± 9	For 10 patients /18 Dose difference: PTV (D <sub>98%</sub> )< 1.2% γ * = 91.6% γ* = 97.1%
	Cervix	14	♦ / 3D Echo with Dixon					32 (prostate patients) / 14	<b>MAE [HU]</b> Body = 59 ± 6	<b>ME [HU]</b> Body = 4 ± 10	For 10 patients /14 Dose difference: PTV (D <sub>98%</sub> ) < 1% γ * = 90.6% γ ** = 97.1%

Xiang et al., 2018 [6]	Prostate	22	1.5 T Siemens / T1	N3 correction algorithm + histogram matching + intensity normalization	DECNN/ DR and RR / 2D	L2	-	21 (Leave- one-out) / 22	MAE [HU] Body = 42.5 ± 3.1		Body = 42.5 ± 3.1		PSNI Body = 0	<b>R [dB]</b> = 33.5 ± .8	/		
Florkow et al., 2019 [48]	Prostate	23	3 T Philips / T1	/	U-Net / DR / 2D	L1	-	16 (3- fold cross- validatio n) / 23	MAE [HU] Body = 34.1 ± 7.9	ME [HU] Body = - 1.2 ± 4.6	<b>PSNR</b> [dB] Body = 34.7 ± 1.7	<b>DSC</b> Bone = 0.78 ± 0.10	/				
Florkow et al., 2019 [49]	Pelvis	24	3 T Philips / echo sequence with Dixon	/	U-Net / RR and DR / 2D	L1	-	11 (3- fold cross- validatio n) / 24	<b>MAE [HU]</b> Body = 27.6 ± 2.6		Bone = 0.	<b>SC</b> = 0.89 ± 02	/				
Fu et al., 2019 [50]	Prostate	20	1.5 T Siemens / 2D T1 TSE	N4 bias field correction algorithm + histogram normalization	CNN / DR / 2D CNN / DR / 3D Han's model [1]	MAE	-	16 / 4	MAE [HU] Body = 40.5 ± 5.4 Body = 37.6 ± 5.1 Body = 41.9 ±		Bone = 0. Bone = 0. Bone = 0.	SC = 0.81 ± 04 = 0.82 ± 04 = 0.80 ± 05	/				
Largent et al., 2019 [51]	Prostate	39	3 T Siemens / 3D T2 SPACE	Normalization and correction of image nonuniformity	U-Net / RR and DR / 2D	L2	-	25 (3- fold cross- validatio n) / 39	MAE [HU] Body = 34.4 ± 7.7		<b>MAE [HU]</b> Body = 34.4 ± 7.7		<b>MAE [HU]</b> Body = 34.4 ± 7.7		ME Body = 14	<b>[HU]</b> = -1.0 ± 4.2	Mean dose difference < 0.6% (PTV and OARs) $\gamma^{\Box} = 99.2\%$

					GAN / RR and DR / 2D	L2 + adversarial loss	Binary cross entropy		Body = 7	= 34.1 ± 7.5	Body	/ = -1.1 ± 13.7	Mean dose difference < 0.6% (PTV and OARs) $\gamma^{\Box} = 99.1\%$
Lei et al., 2019 [11]	Prostate	20	♦       Siemens       / 3D T2       SPACE	N3 correction algorithm + intensity normalization	Cycle-GAN / RR / 3D	Combination mean P distance of adversarial loss and distance loss gradient	MAD	19 (Leave- one-out) / 20	<b>MAE [</b> 50.8 ±	<b>HU]</b> 15.5	<b>PSNR</b> [dB] 24.5 ± 2.6	DSC Air = 0.75 ± 0.06 Bone = 0.81 ± 0.05	/
						difference		20/10	42.3 ±	15.5	23.9 ± 2.0	/	
					DCNN / RR / 3D	Combination mean P distance of adversarial loss and distance loss gradient difference		16 (Leave-	MAE [HU] Body = 59.0 ± 18.6	<b>PSNR</b> [dB] Body = 23.7 ± 3.0	<b>DSC</b> Bone = 0.81 ± 0.06	HD 95% [mm] Bone = 4.9 ±1.5	Protontherap y Mean absolute dose difference = 0.23%
Liu et al., 2019 [52]	Prostate	17	1.5 T Siemens / T2	/	GAN / RR / 3D	Combination mean P distance of adversarial loss and distance loss gradient difference	MAD	one-out) / 17	Body = 74.7 ± 20.0	Body = 22.1 ± 2.7	Bone = 0.81 ± 0.06	Bone = 4.7 ± 1.4 mm	PTV DVH points difference < 1.5% Rectum DVH difference <
					cycle-GAN / RR / 3D	Combination of mean P distance		16 (leave one out)	Body = 51.3	24.2 ± 2.46	Bone = 0.85	4.2 ± 1.0	Bladder DVH

						(MPS: Ip norm) and gradient difference		/ 17	± 16.9 HU	dB	±(	0.05	mm	difference < 11% Mean of absolute maximum range shift: 2.3 ± 2.5 mm γ□ = 92.4% γ * = 98.0% γ** = 99.0%
<b>Stadelmann et al., 2019</b> [53]	Pelvis	42	3 T Philips / 3D FFE mDixon	/	U-Net and LinkNet / RR / 2D	L1 loss	-	27 / 15		M	<b>AE [Hl</b> 41.4	[1		/
Bahrami et al., 2020 [54]	Male Pelvis	15 (+4 additional patient for	3 T Siemens Skyra /	N4 correction algorithm + intensity	eCNN / DR / 2D	MAE		15 (5- fold cross validatio	MAE [HU] Body = 38 ± 5.6	ME [HU] Body = 6 ± 13.4	<b>PS</b> <b>NR</b> <b>[dB</b> <b>]</b> Bo dy = 29. 5 ± 1.3	SSIM Body = 0.96	DS C Bon e = 0.77 ± 0.03	/
r1		evaluation)	3D T2	normalization	U-Net	MAE		n) / 4	MAE [HU] Body = 46 ± 5.7	ME [HU] Body = 6.2 ± 17.9	<b>PS</b> <b>NR</b> <b>[dB</b> <b>]</b> Bo dy = 27.	<b>SSI</b> <b>M</b> Bod y = 0.95	<b>DSC</b> Bon e = 0.7 ± 0.09	/

											4 ± 0.6					
Bird et al., 2020 [55]	Ano- rectal	90 (73 rectum and 17 anus)	1.5 T Siemens / T2 SPACE	CT & MR voxels outside the patient external contour set to an intensity of 1024 and 0 respectively	cGAN / DR and RR / 2D	Focal regression loss	Focal regression loss	46 / 44	MA Defo regis Body F regis Body	E [HU] prmable stration: / = 35.1 Rigid stration: / = 44.5		Deformable registration: Body = 0.4 Bone = -95.5 Rigid registration: Body = 0.8		Deformable registration: Body = 0.4 Bone = -95.5 Rigid registration: Body = 0.8		$\begin{array}{c} \text{Dose} \\ \text{differences:} \\ \text{PTV Rectum} \\ (D_{95\%}, D_{50\%} \\ \text{and } D_{2\%}) < \\ 0.7\% \\ \text{PTV Anus} \\ (D_{95\%}, D_{50\%} \\ \text{and } D_{2\%}) < \\ 0.5\% \\ \gamma \square = 99.5\% \\ \gamma * = 99.8\% \\ \gamma * = 100\% \end{array}$
Brou Boni et al., 2020 [56]	Male pelvis	19 male pelvis from Gold Atlas data set [57]	1.5 T Siemens / T2 TSE, 3 T GE Discover y / T2 FRFSE + 3 T Signa GE / T2 FRFSE	/	cGAN / DR / 2D	L1+ Pearson divergence + adversarial loss	Least square loss	From Gold Atlas data set 11 / 8	MA Body =	<b>E [HU]</b> = 48.5 ±	6	ME [H Body =	I <b>U]</b> -18.3	DVH points difference for PTV, rectum wall, bladder wall, femoral heads < 1.4%		
Cusumano et al., 2020 [39]	Pelvis and abdomen	60 pelvis / 60 abdominal	0.35 T MRIdian / T2/T1 image: TrueFISP	/	cGAN (pix2pix) / DR / 2D	adversarial loss +λ·L1 with λ = 100	PatchGAN loss	80/20	MA Body 1	<b>E [HU]</b> = 54.3 <del>1</del> 1.9	±	<b>ME [H</b> Body = 8.6	IU] 1.4 ±	Dose difference: PTV $(D_{98\%}, D_{50\%}, D_{2\%}) < 0.07$ Gy Rectum $(D_{98\%}, D_{50\%}, D_{2\%}) < 0.05$ Gy $\gamma \Box = 89.3\%$		

													$\gamma ^{*} = 99.0\%$ $\gamma ^{**} = 99.9\%$
										PSI [dl	NR B]	MSE [100 HU²]	
Fetty et al., 2020 [58]	Pelvis (male pelvis + cervix)	40 prostate + 11 cervix + 19 male pelvis from Gold Atlas data set [57]	0.35 T Siemens Magneto m / 2D T2 TSE + 1.5 T Siemens / T2 TSE, 3 T GE Discover y / T2 FRFSE + 3 T Signa GE / T2 FRFSE	N4 bias field correction algorithm	cGan (Pix2Pix): 4 tested networks: SE- ResNet, U- Net, Embedded Net / RR and DR / 2D	L1 + adversarial loss	PatchGAN loss	25 / 10 +18 (19 with 1 patient excluded ) from Gold Atlas data set [57]	MAE [HU] 4 tested networks 0.35 T Body = $41.2 \pm 3.7$ 1.5 T Body = $52.0 \pm 5.5$ 3 T Discovery Body = $43.7 \pm 6.2$ 3 T Signa Body =	[dl 4 tes netwo 0.33 Bod 31.4 1.5 Bod 29.3 1.1 3 Disco y Boo 31.7 1. 3	<b>B</b> ] sted forks 5 T 4y = 5 T 4y = $3 \pm$ 0 7 7 7 7 7 7 7 7	[100 HU <sup>2</sup> ] 4 tested networks 0.35 T Body = 124.9 ± 29.6 1.5 T Body = 201.4 ± 53.3 3 T Discover y Body = 133.1 ± 35.0 3 T	DVH points difference: D <sub>98%</sub> , D <sub>50%</sub> , D <sub>2%</sub> for PTV, rectum, bladder and femoral heads < 1.5%
									48.2 ± 4.9	Sig Bod 30.8 1.1	na ly = 8 ± .2	Signa Body = 146.2 ± 45.9	

Additional table 4: Synthetic-CT generation from pelvis MRI in the literature: summary of data, deep learning architecture, and image and dose evaluations  $\gamma \Box = 1\%/1$  mm gamma pass-rate 1%/1mm;  $\gamma = 2\%/2$  mm gamma pass-rate;  $\gamma = 3\%/3$  mm gamma pass-rate;  $\Rightarrow =$  not specified in the study

Abbreviations: LF = Loss Function; MAE = Mean Absolute Error; ME = Mean Error; DSC = Dice Similarity Coefficient; PSNR = Peak to Signal-to-Noise Ratio; NCC = Normalized Cross-Correlation; MSE = Mean Square Error; MASD = Mean Absolute Surface Distance; HD = Hausdorff Distance; MAD = mean absolute distance, RR = Rigid Registration; DR = Deformable Registration; DCNN = Deep CNN ; FCN = Fully convolution network.

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